Remarks/Arguments

As an initial matter, Applicants note that claims 5-8, 10-22, 25-39, 41, 43, 45-70, and 72-91 were pending in the application as of the mailing date of the Office Action. These claims were presented in the preliminary amendment submitted by applicants and confirmed by the Office Action. *See* Preliminary Amendment dated January 30, 2006; Office Action, page 2. Further, the Office acknowledged the pendency of the claims in the claims worksheet and fee determination record entered into the file after the submission of the preliminary amendment. *See* Claims Worksheet dated February 2, 2006; Fee Determination Record dated February 2, 2006. However, the Office Action erroneously states that only claims 5-8, 20-22, 25-39, 41, 43, 45-70 and 72-91 were pending in the application. *See* Office Action, page 2. The Office has apparently examined claim 19 in addition to the claims listed, but has not examined claims 10-18. Applicants respectfully request that the Office examine claims 10-18.

Claims 5-7, 10, 12-14, 16-22, 25-28, 30, 32-35, 37, 39, 41, 43, 45-70, 72-86, and 89-91, as amended, now appear in the application for the Examiner's review and consideration. Claims 8, 11, 15, 29, 31, 36, 38, 87, and 88 have been canceled without prejudice. Applicants reserve the right to pursue the subject matter of these claims in a subsequent continuation, divisional, or continuation-in-part application. Claim 10 has been amended to recite a process for preparing hydrates of ondansetron hydrochloride Form A from ethanol/isopropanol, chloroform, and chloroform/water. The amendment is supported on page 16, lines 20-25 and page 17, line 28 to page 18, line 25 of the application. Claim 16 has been amended to recite a process for preparing ondansetron hydrochloride hydrates with levels of hydration between that of the monohydrate and the dihydrate. The amendment is supported on page 20, line 19 to page 21, line 27 of the application. Claim 25 has been amended to present the claim in better form. The amendment is supported on page 9, line 22 to page 10, line 2 of the application. Claims 21-22, 30, 32, 39, 41, 43, 46, 49-51, 57-59, 68, 74-77, 82, and 84-86 have been amended for clarity and to correct typographical errors. No new matter has been added to these claims. Claim 83 has been amended to replace the term "substantially dry" with "no more than 0.5% water." This amendment is supported on page 9, lines 28-30 of the application. Claims 89-91 have been amended

to depend from claims 39, 41, and 43. These amendments are supported on page 9, lines 10-17 and page 14, lines 10-16 of the application.

Claims 89-91 have been rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking in enablement. Applicants respectfully traverse.

To fulfill the enablement requirement of 35 U.S.C. § 112, first paragraph, the patent must disclose enough information about the claimed invention to enable one skilled in the art to make and use it without undue experimentation. *In re Wands,* 858 F.2d 731 (Fed. Cir. 1988); M.P.E.P. § 2164.01. A specification "must be taken as in compliance with the enabling requirement of § 112 unless there is reason to doubt the objective truth of the statements contained therein." *In re Marzocchi*, 439 F.2d 220, 224 (C.C.P.A. 1971).

The Office asserts that the claims lack enablement because the specification provides no "information about which polymorphic form in the pharmaceutical composition is effective regarding its bioavailability, drug absorption, rate of dissolution, elimination rate, and stability during the preparations." Office Action, p. 3. The Office argues that many polymorphs have varying dissolution rates, which can lead to differences in bioavailability and result in "potential bio-inequivalence among the several forms of the drug." *Id.*. The Office does not cite any literature to support these assertions. Thus, the evidence offered by the Office is no more than mere conjecture, and is not sufficient to establish reason to doubt that Applicants' disclosure would have enabled one of skill in the art to make and use the claimed invention at the time of filing. The Office Action argues the effectiveness of the drug, but does not set forth any objective data that the polymorph has a different bioequivalency. Applicants further point out that none of the *In re Wands* factors are considered in the Office Action. Therefore, the rejection of claims 89-91 under 35 U.S.C. § 112, first paragraph as allegedly lacking in enablement cannot stand and should be withdrawn.

Claims 45, 66, and 83 have been rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite. Applicants respectfully traverse.

"Determining whether a claim is definite requires an analysis of whether one skilled in the art would understand the bounds of the claim when read in light of the specification." *Solomon v. Kimberly-Clark Corp.*, 216 F.3d 1372, 1378 (Fed. Cir. 2000) (citing *Personalized Media Comm., LLC v. ITC*, 161 F.3d 696, 705 (Fed. Cir.

1998)). When the specification states the meaning that a term in the claim is intended to have, the claim is examined using that meaning. *In re Zletz*, 893 F.2d 319 (Fed. Cir. 1989); M.P.E.P. § 2173.05(a).

The Office alleges that claims 45 and 66 are indefinite because "the claims are directed to the anhydrous hydrochloride compound, but it contains water." Office Action, p. 4, ll. 7-8.

As to claim 45, the specification states: "Ondansetron hydrochloride Form B anhydrous of the present invention absorbs up to 2% moisture when exposed to 60% relative humidity. The water absorbed by the crystal is not within the crystal structure of a hydrous form as a hydrate water." *See* Specification, p. 9, ll. 1-4. The language of the specification gives a precise definition to the language of claim 45, *i.e.*, an anhydrous ondansetron hydrochloride Form B with about 2% water absorbed outside of the crystal structure. As such, one of skill in the art would understand the bounds of claim 45 when reading it in light of the definition given in the specification.

As to claim 66, the specification states: "Ondansetron hydrochloride Form E contains 1.8%-2.0% water, as measured by Karl Fisher. This is a stoichiometric value corresponding to 1/3 molecule of water per molecule of ondansetron hydrochloride." *See* Specification, p. 12, ll. 13-16. The specification further states: "[O]ndansetron hydrochloride isopropanolate Form E when exposed up to 60% relative humidity for one week can contain water up to 10% without modifying its crystal structure." *See id.* at p. 12, l. 30 to p. 13, l. 1. From this description, one of skill in the art would understand Form E to be a hydrate, which can contain up to 10% water. As such, one of skill in the art would understand the bounds of claim 66 when reading it in light of the specification.

The Office alleges that claim 83 is indefinite because "the specification does not elaborate what is meant by the terms 'substantially dry.'" Office Action, p. 4, ll. 11-13. This rejection has been rendered moot by the amendment of claim 83.

Based on the foregoing, the rejection of claims 45, 66, and 83 under 35 U.S.C. § 112, second paragraph cannot stand and should be withdrawn.

Claims 5-7 and 19-20 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Chinese Patent No. 1113234 to Guosheng, et al. ("CN '234"). Applicants respectfully traverse.

To anticipate a claim, a single reference must disclose the claimed invention with sufficient clarity to prove its existence in the prior art, and must disclose every element of the challenged claim. *Motorola Inc. v. Interdigital Technology Corp.*, 43 U.S.P.Q.2d 1481, 1490 (Fed. Cir. 1997); *PPG Industries Inc. v. Guardian Industries Corp.*, 37 U.S.P.Q.2d 1618, 1624 (Fed. Cir. 1996). Absence from the reference of any claimed element negates anticipation. *Kloster Speedsteel AB v. Crucible Inc.*, 231 U.S.P.Q. 160 (Fed. Cir. 1986). In order to anticipate claims under 35 U.S.C. § 102, a reference must also provide an enabling disclosure of the subject matter of the claims. *See, e.g., In re Collins*, 462 F.2d 538, 542 (C.C.P.A. 1972).

CN '234 discloses a class of ondansetron hydrochloride hydrates. *See* CN '234, description p. 1 (Formula (I)). CN '234 also discloses a process for preparing ondansetron hydrochloride monohydrate by drying ondansetron hydrochloride dihydrate under vacuum with heating in the presence of the desiccant P_2O_5. *See* CN '234, description pp. 8-10 (Embodiments A_1 and A_2).

Claims 5-7 recite processes for the preparation of ondansetron hydrochloride monohydrate that involve contacting crystals of ondansetron hydrochloride dihydrate with a mixture of from about 4% to about 50% water in ethanol to convert the dihydrate to ondansetron hydrochloride monohydrate. Claims 19-20 recite anhydrous ondansetron hydrochloride and anhydrous ondansetron hydrochloride Form B, respectively. CN '234 does not disclose the use of an ethanol/water mixture to convert the dihydrate to the monohydrate, as recited in claims 5-7. Further, CN '234 does not disclose anhydrous ondansetron hydrochloride, as recited in claims 19-20. Since CN '234 does not disclose each and every element of the claims, the legal standard for anticipation has not been satisfied.

Claims 62-65 have been rejected under 35 U.S.C. § 102(b) as allegedly inherently anticipated by U.K. Publication No. 2 153 821 to Coates, et al. ("GB '821"). Applicants respectfully traverse.

"[A] prior art reference may anticipate without disclosing a feature of the claimed invention if that missing characteristic is necessarily present, or inherent, in the single anticipating reference." *SmithKline Beecham Corp. v. Apotex*, 403 F.3d 1331, 1343 (Fed. Cir. 2005); *Schering Corp. v. Geneva Pharmaceuticals, Inc.*, 339 F.3d 1373, 1377 (Fed. Cir. 2003); *Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1268 (Fed. Cir. 1991). Inherent anticipation requires that the prior art contain

the missing characteristic each and every time. *See SmithKline Beecham Corp.*, 403 F.3d at 1343 (emphasis added). In order to support an anticipation rejection on the basis of inherency, the Office must "provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the prior art." *Ex parte Levy*, 17 U.S.P.Q.2d 1461, 1464 (Bd. Pat. App. & Interfer. 1990) (emphasis omitted); *see also* M.P.E.P. § 2112(IV).

The Office argues that GB '821 anticipates claims 62-65 because it "teaches the preparation of producing ondansetron hydrochloride using isopropanol solvent" in Example 10 and "[o]ndansetron hydrochloride Form E mono- and/ or hemi-isopropanolate is inherently formed during the process." *See* Office Action, p. 6.

Example 10 of GB '821 discloses the preparation of ondansetron hydrochloride dihydrate by recrystallization from a mixture of water and isopropanol. GB '821, p. 16, ll. 1-12. GB '821 discloses water assay data (10.23% water) to support its assertion that the product of Example 10 is ondansetron hydrochloride dihydrate. *Id.* The Office has not provided any basis in fact or technical reasoning to doubt this assertion.

Claims 62-65 recite isopropanol solvates of ondansetron hydrochloride, and not ondansetron hydrochloride dihydrate. According to the specification, the claimed isopropanol solvates may contain 1.8%-2.0% water by Karl Fisher, rather than 10.23% water as recited in GB '821. *See* Application, page 12, lines 13-14. Because GB '821 discloses a process that produces the dihydrate each and every time, rather than the claimed isopropanol solvates, the legal standard for inherent anticipation has not been satisfied.

Claims 72-73 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Merck Index, 12th ed., p. 6977 ("Merck Index"). The Office argues that the Merck Index anticipates the claims because it "teaches the preparation of producing Ondansetron hydrochloride using methanol solvent." *See* Office Action, pp. 6-7.

The Merck Index discloses that the product obtained by recrystallization from methanol is ondansetron free base, citing U.S. patent No. 4,695,578 ("'578 patent"), which characterizes the product as such by melting point. Again, the Office has not provided any basis in fact or technical reasoning to doubt this assertion.

Claims 72-73 recite methanol solvates of ondansetron hydrochloride, and not ondansetron free base. Therefore, the product produced by the process disclosed in the Merck Index is not that of the claims. Because the Merck Index discloses a process that produces the free base each and every time, rather than the claimed methanol solvates, the legal standard for inherent anticipation has not been satisfied.

The Office rejects claims 5-8, 20-22, 25-39, 41, 43, 45-70, and 72-91 under 35 U.S.C. § 103(a) as allegedly obvious over CN '234 in view of Llacer, et al., *International Journal of Pharmaceutics*, 177 (1999), pp. 221-229 ("Llacer article"). The rejection has been rendered moot as to claims 8, 29, 31, 36, 38, 87, and 88 by the cancellation of those claims. As to the remaining claims, Applicants respectfully traverse.

The Federal Circuit in *In re Dembiczak*, 175 F.3d 994 (Fed. Cir. 1999), set forth three requirements to make out a *prima facie* case of obviousness under 35 U.S.C. § 103(a) in view of the prior art. In order for a claim to be *prima facie* obvious, the Office must establish: (i) a teaching or suggestion in the prior art to modify or combine references to form the claimed invention, (ii) a reasonable expectation of success taught or suggested in the prior art, and (iii) all of the elements of the claimed invention are found in the prior art. *Id.*; *see also* M.P.E.P. § 2143. The Office can satisfy its burden to establish a *prima facie* case of obviousness based on a combination of references "only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references." *In re Fritch*, 972 F.2d 1260, 1265, 23 U.S.P.Q.2d 1780, 1783 (Fed. Cir. 1992). The need for specificity is paramount. *In re Sang Su Lee*, 277 F.3d 1338, 1343, 61 U.S.P.Q.2d 1430 (Fed. Cir. 2002).

The Office asserts that CN '234 teaches a general procedure for producing ondansetron hydrochloride with an aqueous solvent by dissolving ondansetron in a water/alcohol solvent and adding hydrogen chloride to produce ondansetron hydrochloride, citing Embodiment A_1 of CN '234. Office Action, p. 9, ll. 14-19. However, Embodiment A_1 discloses a process for preparing ondansetron hydrochloride dihydrate encompassing the steps of mixing ondansetron free base with ethyl acetate, heating the mixture, eluting the product through a silica column with ethyl acetate, 1N HCl, and water in succession, concentrating the aqueous solution

collected, and cooling to crystallize the ondansetron hydrochloride dihydrate. CN '234, description p. 8, ll. 5-24.

The Llacer article discloses processes for the preparation of polymorphs of ondansetron free base by recrystallization from acetone, chloroform, benzene, cyclohexane, ethanol, and methanol. *See* Llacer article, p. 222 (Table 1).

As to claims 5-7, CN '234 discloses a process for preparing the monohydrate by drying the dihydrate under vacuum in the presence of the desiccant P_2O_5, rather than by exposure to a mixture of water and ethanol as recited in the claims. The skilled artisan recognizes that P_2O_5 is used to remove water. Thus, the disclosures of CN '234 would not provide the skilled artisan with a reasonable expectation of success in using water to convert the dihydrate to the monohydrate. The Llacer article cannot remedy the deficiencies of CN '234 because the Llacer article does not disclose ondansetron hydrochloride at all, let alone ondansetron hydrochloride hydrates. Nor does the Llacer article disclose any method for preparing ondansetron hydrochloride or ondansetron hydrochloride hydrates. Further, the Office has not pointed to any motivation to combine the teachings of CN '234 and the Llacer article to arrive at the claimed invention. CN '234 discloses crystalline forms of ondansetron hydrochloride from water, while the Llacer article discloses crystalline forms of ondansetron free base from organic solvents. There is nothing in the references to teach or suggest that procedures suitable for producing crystalline ondansetron free base would be suitable for producing crystalline ondansetron hydrochloride. In fact, the Office even admits that different crystalline forms of a compound exhibit different properties. *See* Office Action, p. 3.

Claims 19-22, 39, 41, 43, 45, and 89-91 recite anhydrous ondansetron hydrochloride, anhydrous ondansetron hydrochloride Form B, and pharmaceutical compositions thereof. Claims 25-28, 30, 32-35, 37-38, 46-48, and 82-86 recite processes for preparing these anhydrous forms. CN '234 does not disclose anhydrous ondansetron hydrochloride or any process for preparing anhydrous ondansetron hydrochloride. As noted above, the only dehydrating method disclosed in CN '234 dehydrates ondansetron hydrochloride dihydrate to obtain the monohydrate. *See* CN '234, p. 8, 10. This disclosure does not teach or suggest the complete dehydration of the dihydrate or monohydrate. In fact, because CN '234 does not completely dehydrate the dihydrate under strong dehydrating conditions, one of skill in the art

would not have a reasonable expectation of success in being able to obtain the anhydrous form at all. The Llacer article cannot remedy the deficiencies of CN '234 because the Llacer article does not disclose ondansetron hydrochloride, let alone the anhydrous form. Moreover, the Llacer article does not disclose methods for making ondansetron hydrochloride or the anhydrous form. Further, as discussed above, the Office has not pointed to any motivation to combine these two references.

Claims 49, 50, 52, 57-58, 62-67, and 72-76 recite ondansetron hydrochloride Forms C, D, E, H, and I, as well as methanol and isopropanol solvates of ondansetron hydrochloride. Claims 51, 53-56, 59-61, 68-70, and 77-81 recite processes for preparing these forms. CN '234 does not disclose ondansetron hydrochloride Forms C, D, E, H, or I, let alone processes for preparing them. Further, CN '234 does not disclose methanol or isopropanol solvates of ondansetron hydrochloride. In fact, the only solvates disclosed by CN '234 are hydrates. One of skill in the art would not be motivated to develop the claimed polymorphs and solvates of ondansetron hydrochloride by CN '234's bare disclosure of ondansetron hydrochloride hydrates. At most, CN '234 could provide the skilled artisan with an invitation to try to isolate different solvates, but obvious to try is not the legal standard for obviousness under § 103. *See, e.g., In re O'Farrell*, 853 F.2d 894 (Fed. Cir. 1988). The Llacer article cannot remedy the deficiencies of CN '234 because it does not disclose ondansetron hydrochloride at all, let alone the claimed polymorphs and solvates. In addition, as discussed above, the Office has not pointed to any motivation to combine these two references.

Based on the foregoing arguments, the rejection of claims 5-8, 20-22, 25-39, 41, 43, 45-70, and 72-91 under 35 U.S.C. § 103(a) as obvious over CN '234 in view of the Llacer article cannot stand and should be withdrawn.

The Office also rejects claims 5-8, 20-22, 25-39, 41, 43, 45-70, and 72-91 under 35 U.S.C. § 103(a) as allegedly obvious over GB '821 in view of the Llacer article. The rejection has been rendered moot as to claims 8, 29, 31, 36, 38, 87, and 88 by the cancellation of those claims. As to the remaining claims, Applicants respectfully traverse.

The Office asserts that GB '821 "teaches the preparation of producing Ondansetron hydrochloride using various solvents," citing Examples 1a and 10 of GB '821. Office Action, p. 12, ll. 1-21. However, Example 1a of GB '821 discloses the

recovery of ondansetron hydrochloride by recrystallization from absolute ethanol (*See* GB '821, p. 7, ll. 55-65) and Example 10 discloses the recovery of ondansetron hydrochloride dihydrate by recrystallization from a mixture of water and isopropanol.

As to claims 5-7, directed to processes for preparing ondansetron hydrochloride monohydrate, GB '821 discloses a process for preparing the dihydrate by recrystallization from a mixture of water and isopropanol. GB '821 does not, however, disclose or suggest a process for recovery of the monohydrate. The Llacer article cannot remedy the deficiencies of GB '821 because the Llacer article does not disclose ondansetron hydrochloride hydrates or any method of preparing them.

As to product claims 19-22, 39, 41, 43, 45, and 89-91 and process claims 25-28, 30, 32-35, 37-38, 46-48, and 82-86, directed to anhydrous ondansetron hydrochloride, GB '821 does not disclose anhydrous ondansetron hydrochloride or any process for preparing anhydrous ondansetron hydrochloride. Further, GB '821 does not even teach or suggest that the anhydrous form exists. Thus, GB '821 cannot teach or suggest the limitations of the claims to the skilled artisan. The Llacer article cannot remedy the deficiencies of GB '821 because the Llacer article does not disclose ondansetron hydrochloride at all, let alone teach or suggest the anhydrous form.

As to product claims 49, 50, 52, 57-58, 62-67, and 72-76, and process claims 51, 53-56, 59-61, 68-70, and 77-81, directed to polymorphs and solvates of ondansetron hydrochloride, GB '821 does not disclose ondansetron hydrochloride Forms C, D, E, H, or I, let alone processes for preparing them. Further, GB '821 does not disclose methanol or isopropanol solvates of ondansetron hydrochloride. In fact, the only solvates disclosed by GB '821 are hydrates. Thus, GB '821 cannot teach or suggest the limitations of the claims. The Llacer article cannot remedy the deficiencies of GB '821 because it does not disclose ondansetron hydrochloride at all, let alone the claimed polymorphs and solvates.

Based on the foregoing arguments, the rejection of claims 5-8, 20-22, 25-39, 41, 43, 45-70, and 72-91 under 35 U.S.C. § 103(a) as obvious over GB '821 in view of the Llacer article cannot stand and should be withdrawn.

The Office rejects claims 5-8, 20-22, 25-39, 41, 43, 45-70, and 72-91 under 35 U.S.C. § 103(a) as allegedly obvious over EP 0 415 522 to Collin, et al. ("EP '522") in view of the Llacer article. The rejection has been rendered moot as to claims 8, 29,

31, 36, 38, 87, and 88 by the cancellation of those claims. As to the remaining claims, Applicants respectfully traverse.

The Office asserts that "Collin does teach the general procedure for producing Ondansetron hydrochloride using the aqueous alcoholic solvent," citing Example 1 of EP '522. Office Action, pp. 14-16. However, Example 1 of EP '522 recites a process for producing ondansetron hydrochloride dihydrate wherein the crystals are less than 250 microns in size by the following general steps: preparing a solution of ondansetron in a mixture of isopropanol, water, and glacial acetic acid, treating the solution with hydrochloric acid at 70°C, cooling the solution, filtering the resulting suspension to obtain a solid, washing the solid with isopropanol, drying the solid under vacuum with heating, and exposing the dried solid to humid air to obtain ondansetron hydrochloride dihydrate with crystals of less than 250 microns in size. *See* EP '522, p. 3, ll. 15-44.

As to claims 5-7, directed to processes of preparing the ondansetron hydrochloride monohydrate, EP '522 discloses a process for preparing the dihydrate by exposing ondansetron hydrochloride to a humid atmosphere. EP '522 does not disclose or suggest the recovery of the intermediate monohydrate. The Llacer article cannot remedy the deficiencies of EP '522 because the Llacer article does not disclose ondansetron hydrochloride hydrates or any method of preparing them. Further, the Office has not pointed to any motivation to combine the teachings of EP '522 and the Llacer article to arrive at the claimed invention. EP '522 discloses crystalline forms of ondansetron hydrochloride from a mixture of water and isopropanol, while the Llacer article discloses crystalline forms of ondansetron free base from organic solvents. There is nothing in the references to teach or suggest that procedures suitable for producing crystalline ondansetron free base would be suitable for producing crystalline ondansetron hydrochloride.

As to product claims 19-22, 39, 41, 43, 45, and 89-91 and process claims 25-28, 30, 32-35, 37-38, 46-48, and 82-86, directed to anhydrous ondansetron hydrochloride, EP '522 discloses a method for de-solvating ondansetron hydrochloride by drying under heat and/or vacuum. *See* EP '522, pp. 3-5, Examples 1-4. EP '522 does not disclose whether this process produces anhydrous ondansetron hydrochloride. By focusing on drying, however, EP '522 would not motivate one of skill in the art to use solvent to dehydrate ondansetron hydrochloride, as recited in the

claims. The Llacer article cannot remedy the deficiencies of EP '522 because the Llacer article does not disclose anhydrous ondansetron hydrochloride or any method of preparing it. Further, as discussed above, the Office has not pointed to any motivation to combine the teachings of EP '522 and the Llacer article.

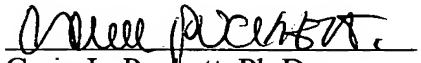
As to product claims 49, 50, 52, 57-58, 62-67, and 72-76, and process claims 51, 53-56, 59-61, 68-70, and 77-81, directed to polymorphs and solvates of ondansetron hydrochloride, EP '522 does not disclose ondansetron hydrochloride Forms C, D, E, H, or I, let alone processes for preparing them. Further, EP '522 does not disclose methanol or isopropanol solvates of ondansetron hydrochloride. In fact, the only solvate disclosed by EP '522 is the dihydrate. One of skill in the art would not be motivated to develop the claimed polymorphs and solvates of ondansetron hydrochloride by EP '522's bare disclosure of ondansetron hydrochloride dihydrate. As discussed above, at most this type of disclosure could provide the skilled artisan with an invitation to try to isolate different solvates. The Llacer article cannot remedy the deficiencies of EP '522 because it does not disclose ondansetron hydrochloride at all, let alone the claimed polymorphs and solvates. In addition, as discussed above, the Office has not pointed to any motivation to combine these two references.

Based on the foregoing arguments, the rejection of claims 5-8, 20-22, 25-39, 41, 43, 45-70, and 72-91 under 35 U.S.C. § 103(a) as obvious over EP '522 in view of the Llacer article cannot stand and should be withdrawn.

In view of the foregoing amendments and remarks, Applicants respectfully submit that the present application is in condition for allowance. Early and favorable action by the Examiner is earnestly solicited. If any outstanding issues remain, the Examiner is invited to telephone the undersigned at the telephone number indicated below to discuss the same. No fee is believed to be due for the submission of this response. Should any fees be required, please charge such fees to Kenyon & Kenyon LLP Deposit Account No. 11-0600.

Respectfully submitted,

KENYON & KENYON LLP

Dated: October 11, 2006 By: 

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